

REMARKS

Applicants respectfully request reconsideration of the subject application. No claims have been amended, added, or canceled. Claims 1-22, 24-26, 28, and 29 are withdrawn from consideration. No new matter has been added.

Applicants reserve all rights under the doctrine of equivalents.

Accompanying this response is a Declaration of Benjamin Davis under 37 C.F.R. § 1.132 (dated May 6, 2011). Mr. Davis is one of the inventors of the present patent application.

Claim Rejections – 35 U.S.C. § 103

Claims 23, 31, and 32 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over B.G. Davis et al. et al. Tetrahedron: Asymmetry (2000) 11, pages 245-262, (hereinafter “Davis”), L. Engman et al. Tetrahedron (1994) 50(9), pages 2929-2938, (hereinafter “Engman”), H.S. Hsieh et al. Biochemistry (1975) 14(8), pages 1632-1636, (hereinafter “Hsieh”), and U.S. Patent/Publication No. 5,759,823 by Wong, (hereinafter, “Wong”).

Davis discloses preparing glycomethanethiolsulfonate (glycol-MTS) protein glycosylation reagents. The reagents are used in a controlled site-selective glycosylation strategy that combines site-directed mutagenesis with chemical modification. Davis, however, does not disclose reagents that contain selenium.

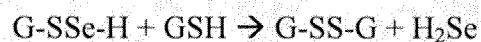
Engman discloses an investigation of a glutathione peroxidase-like catalysis of α -(phenylselenenyl) ketones. In particular, Engman discloses reacting S-(phenylselenenyl)glutathione with a further glutathione to form G-S-S-G, where G denotes

glutathione residue (see Scheme 3 on page 2931 of Engman). For example, Engman discloses the following reaction:



Glutathione is a peptide, which contains a cysteine residue, and is not a carbohydrate residue.

Similar to Engman, Hsieh also discloses reacting S-(phenylselenenyl)glutathione with a further glutathione to form G-S-S-G, where G denotes glutathione residue (see Scheme 3 on page 1635 of Hsieh). For example, Hsieh discloses the following reaction:



Wong discloses oligosaccharide compounds that are substrates and inhibitors of glycosyltransferase and glycosidase enzymes.

Claim 23 reads as follows:

A method of chemically modifying a protein, peptide or amino acid comprising at least one selenenylsulfide group, the method comprising reacting the protein, peptide or amino acid with a carbohydrate compound comprising a thiol group.

(Claim 23)(emphasis added).

The Declaration of Benjamin Davis ("Declaration") declares that Mr. Davis does not believe that Engman and Hsieh would have led one of ordinary skill in the art familiar with Davis to expect that the reaction of the presently claimed invention would be successful. The Declaration further declares that -S- and -Se- are not chemically equivalent, Hsieh discloses forming a gas that is a strong driving force of Hsieh's reaction, and Engman discloses the formation of PhSeSePh. Furthermore, the Declaration declares that the present application illustrates an unexpected success of the claimed reaction.

Applicants respectfully that the combination of Davis, Engman, Hsieh, and Wong does not teach or suggest applicants' claims. In particular, applicants respectfully submit that

Davis, Engman, Hsieh, and Wong do not teach or suggest a combination with each other. The Examiner asserts that combining Davis, Engman, Hsieh, and Wong would be obvious to one of ordinary skill in the art because “while Davis teaches the use of Carb-S-SO₂Me, the artisan would have recognized that alternatives, such as thioglucose (Glc-SH), which is commercially available, as identified by Wong), could be employed in the method” (Office Action, p. 2). Furthermore, the Examiner asserts that the “artisan, in looking to other related art- particularly the art of Engman and Hsieh, show the use of -SePh in the coupling of protein-S-S-R compounds, thus there is ample teaching in the art to lead one to the use of SePh in the coupling reaction ... in order to improve on the method of Davis.”

Applicants respectfully disagree with the Examiner’s motivation for the combination. The Examiner apparently asserts here one of ordinary skill in the art would look to modify the Davis reaction by using reactants that are not disclosed in Davis. Applicants, however, respectfully submit that one of ordinary skill would not look to either Engman or Hsieh to replace the Carb-S-SO₂Me reactant of Davis with either G-SSe-Ph (Engman) or G-SSe-H (Hsieh) because one of ordinary skill would know that -S- and -Se- are not chemically equivalent (See the enclosed Declaration of Benjamin Davis (“Declaration”) at Sec. 5(a) and 5(b)). Because -S- and -Se- are not chemically equivalent, one of ordinary skill in the art would not be motivated to replace the Davis Carb-S-SO₂Me reactant with one of the SSe reactants proposed by the Examiner (*Id.*). Thus, applicants respectfully submit that one of ordinary skill in the art would not look modify the reaction of Davis with the reactants of either Engman or Hsieh.

Furthermore, applicants respectfully submit that one of ordinary skill would not have a reasonable expectation of success based on the disclosures of Hsieh and Davis. “The prior art can be modified or combined to reject claims as *prima facie* obvious as long as there is a

reasonable expectation of success” (MPEP §2143.02(I)). One of ordinary skill in the art would realize that the reaction in the Hsieh publication forms a hazardous gas, namely H_2Se , whereas the Davis reaction does not (Declaration, Sec. 5(d)). Furthermore, this gas formation would be a strong driving force in the Hsieh reaction (*Id.*). Because the Hsieh reaction produces the H_2Se gas that is a strong driving force of the Hsieh reaction and the Davis reaction does not, applicants respectfully submit that one of ordinary skill in the art would not have a reasonable expectation of success based on the disclosures of Hsieh and Davis. Therefore, one of ordinary skill in the art would not look modify the reaction of Davis with the reactant(s) of Hsieh.

With respect to Engman, the Examiner apparently asserts that one of ordinary skill in the art would use Engman’s equation 3 that produces PhSeH to modify the Davis reaction. As stated above, applicants respectfully submit that one of ordinary skill in the art would need a reasonable expectation of success to make the proposed modification (MPEP §2143.02(I)). However, applicants respectfully submit that one of ordinary skill in the art would not have a reasonable expectation of success because one of ordinary skill in the art would not assume that $-\text{Se}-$ and $-\text{SO}_2-$ would have the same reactivity. Because $-\text{Se}-$ and $-\text{SO}_2-$ do not have the same reactivity, one of ordinary skill in the art would not have a reasonable expectation of success and, therefore, one of ordinary skill in the art would not be motivated to modify Davis with the disclosure of Engman.

In addition, the Examiner is required to consider the prior art in its entirety. “A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention.” (MPEP §2141.02(VI)). Applicants respectfully submit that one of ordinary skill in the art would consider the disclosure of Engman as a whole and not just a part of equation 3. Applicants respectfully submit that the driving force

of the reaction shown in the Engman publication is the formation of PhSeSePh (Declaration, Sec. 5(f)). Because an equivalent product cannot be formed in the reactions disclosed in the Davis publication, it would be clear to one of ordinary skill in the art that the reaction in equation 3 of the Engman publication is completely unrelated to the reactions disclosed in the Davis publication (*Id.*).

Applicants respectfully further submit that one of ordinary skill in the art would not look to combine Engman with Davis because of the unexpected success of the claimed reaction. “A *prima facie* case of obviousness based on structural similarity is rebuttable by proof that the claimed compounds possess unexpectedly advantageous or superior properties” (MPEP §2144.09(VII)). Applicants respectfully submit that Engman discloses a maximum expected yield of 50% (Declaration, Sec. 5(g)). In contrast, Applicants’ claimed reaction illustrates a conversion that is over 95% (Applicants’ Specification, Table in Example 19, p. 35). Because one of ordinary skill in the art would have expected a 50% conversion based on the disclosures of Engman, and applicants’ claimed reaction gives a conversion that is over 95%, applicants respectfully submit that applicants’ claimed reaction illustrates an unexpected success. Therefore, applicants respectfully submit that one of ordinary skill in the art would not look to modify the reaction of Davis with the reaction of Engman.

Thus, applicants respectfully submit that one of ordinary skill in the art would not look to combine Davis with Engman and/or Hsieh. Therefore, suggesting that these references are combinable relies of impermissible hindsight based on the applicants’ own disclosure.

Accordingly, claim 23 and claims 31 and 32 that depend on claim 23 are not rendered obvious by Davis, Engman, Hsieh, and Wong.

CONCLUSION

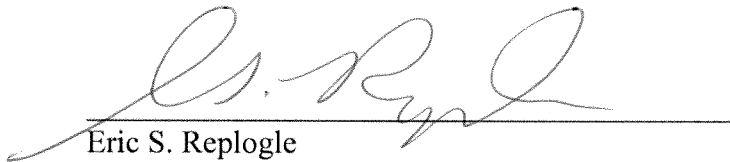
Applicants respectfully submit that the applicable objections and rejections have been overcome. Applicants reserve all rights under the doctrine of equivalents.

Pursuant to 37 C.F.R. 1.136(a)(3), applicants hereby request and authorize the U.S. Patent and Trademark Office to (1) treat any concurrent or future reply that requires a petition for extension of time as incorporating a petition for extension of time for the appropriate length of time and (2) charge all required fees, including extension of time fees and fees under 37 C.F.R. 1.16 and 1.17, to Deposit Account No. 02-2666.

Respectfully submitted,

BLAKELY, SOKOLOFF, TAYLOR & ZAFMAN LLP

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